SYNTHESIS AND CHARACTERIZATION OF REVERSIBLY CORE CROSS-LINKED MICELLES SENSITIVE TO REDUCTIVE ENVIRONMENT

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Over the last decade, polymer micelles attracted an increasing interest in drug pharmaceutical research because they could be used as efficient drug delivery systems[1,2]. Micelles of amphiphilic block copolymers are supramolecular core-shell type assemblies of tens of nanometers in diameter[3].
In principle, the micelles core is usually constructed with biodegradable hydrophobic polymers such as aliphatic polyesters, e.g. poly(ε-caprolactone) (PCL), which serves as a reservoir for the incorporation of various lipophilic drugs. Water soluble poly(ethylene oxide) (PEO) is most frequently used to build the micelles corona because it is very efficient in preventing protein adsorption at surfaces and in stabilizing the micelles in the blood compartment, giving rise to particles invisible to the body defence system (so-called stealthy or long circulating particles)[4]. The tumour targeting of a cytotoxic agent refers to the passive accumulation of polymer nanocarriers to solid tumours (EPR effect) followed by active internalization in tumor cells. The internalization of the drug is required for cell death because most cytotoxic drugs act intracellularly. The building of smart copolymer micelles able to adapt in response to their environment is thus highly desired.
Even if micelles get a high stability in aqueous media, the dissociation of micelles is not always preserved when they are injected in the blood compartment. The reversible cross-linking of the micelles by disulfide bridges will provide the stability of micelles after the administration and will release the drug intracellularly by enzymatic breaking of disulfide bridges.
The synthesis of reversibly cross-linkable PEO-*b*-PCL based copolymers, their micellization and cross-linking in aqueous media together with their biological properties will be presented.

References

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